K042762

DEC 22 2004

510(k) SUMMARY

Pefakit® APC-R Factor V Leiden

In accordance with the requirements of Safe Medical Devices Act (SMDA) of 1990, a 510(k) summary is provided as outlined in 21 CFR 807.92.

Part A

1. Submitter's name, address, telephone number, contact person, and the date the summary was prepared

Submitter's Name:	Pentapharm Ltd.
Submitter's Address:	Engelgasse 109 CH-4002 Basel/Switzerland
Submitter's Telephone Number:	++41 61 706 48 48
Submitter's Contact:	Reto Schöni, PhD Regulatory Affairs Specialist Diagnostics, R&D Hemostasis and Test Kit Development
Date of 510(k) Preparation:	September 30, 2004

2. Name of the device, including the trade or proprietary name, the common or usual name and the classification name

Trade or Proprietary Name:	Pefakit® APC-R Factor V Leiden
Common or Usual Name:	APC Resistance Test
Classification Name:	Hematology, Factor Deficiency Test

3. Identification of the legally marketed device to which the submitter claims substantial equivalence

Predicate Device Name:	COATEST® APC™ RESISTANCE V / COATEST® APC™ RESISTANCE VS
510(k) Number:	K963111
Regulation Number:	864.7925
Regulatory Class:	II

4. Description of the device

Pefakit® APC-R Factor V Leiden is an in vitro diagnostic test kit containing 3 vials each of the following 4 lyophilized reagents:

R1: APC / RVV-V (+APC) Reagent (APC, RVV-V, Polybrene, Hepes, BSA)

R2: APC / RVV-V (-APC) Reagent (RVV-V, Polybrene, Hepes, BSA)

R3: PTA Reagent (Prothrombin Activator, EDTA, Hepes, BSA)

R4: Dilution Plasma (Human Plasma, processed)

For Quality Assurance/Quality Control the corresponding control kit 'Pefakit® APC-R Factor V Leiden Controls' has to be used. It contains 3 vials each of the following 2 lyophilized control plasmas:

C1: pooled human plasma from donors confirmed to be normal wild-type by FV Leiden PCR testing

C2: pooled human plasma from donors confirmed to be heterozygous by FV Leiden PCR testing

5. Statement on the intended use of the device

Pefakit® APC-R Factor V Leiden is a plasma based functional assay for the determination of resistance to activated protein C caused by the factor V Leiden mutation (FV:Q506).

6. Summary of the technological characteristics of the new device in comparison to those of the predicate device

The predicate device COATEST® APC™ RESISTANCE V / COATEST® APC™ RESISTANCE VS is an aPTT-based test which contains purified phospholipids and colloidal silica as contact activator. It makes use of excess FV deficient plasma to enhance the sensitivity of the test. It also contains polybrene to antagonize heparin eventually present in the patient's blood.

The new device Pefakit® APC-R Factor V Leiden also uses FV deficient plasma and polybrene with the same goal. It was shown that not only heparin is antagonized, but also the more and more frequently used heparinoids like low molecular weight heparins (LMWH) or pentasaccharide (PES). In contrast to the predicate device it is prothrombin based. It means that it is not aPTT based and contains no phosphorlipids. This feature makes it insensitive to even high titres of lupus anticoagulants present in the blood of LAC patients. The formation/activation of thrombin from prothrombin present in the patients blood is induced by a specific FVa-dependent and Ca^{2+} -independent prothrombin activator (Noscarin) purified from the venom of the tiger snake Notechis scutatus scutatus. Thus the test is also independent from all other factors influencing the thrombin formation based on the prothrombinase complex.

Discrimination of different patients with different factor V Leiden genotypes is based on a ratio. As for the predicate device this ratio is calculated from the clotting times measured using a reagent containing activated protein C (+APC reagent) and a reagent containing no activated Protein C (-APC reagent). Both reagents are added to

the patient's plasma sample previously diluted with FV deficient plasma. In contrast to the predicate device in the proposed device a specific FV activator (RVV-V) purified from the venom of Russel's Viper (Daboia russelli) activates the FV present in the patients blood, which makes the test also independent from all other factors present in the patients blood influencing FV activation by other means.

Part B

1. Brief discussion of the non-clinical tests submitted, referenced , or relied on in the premarket notification submission for a determination of substantial equivalence

Non-clinical tests were done in-house to determine precision, diagnostic sensitivity and specificity, interferences, stability, and batch-to-batch variability.

The device was shown to have a high precision within the series (20 tests) and from day to day (10 days) on all instruments tested so far, with an overall coefficient of variation (CV) < 6%. This is comparable to what has been claimed for the predicate device. A side-by-side comparison of the precision within the series and from day to day with two devices on the same analyzer (STA® R) within the frame of a clinical study at the Clinical Institute for Medical and Chemical Laboratory Diagnostics (CIMCLD), Allgemeines Krankenhaus (AKH) in Vienna/Austria showed that the precision of both tests is equivalent.

In-house testing showed that the submitted device has a diagnostic sensitivity and specificity of 100%, with a high power of resolution not only between carriers and non-carriers of the FV Leiden mutation, but also between heterozygous and homozygous carriers of this mutation.

The submitted device proved to be insensitive to most interference factors. Those interfering with the test like high factor V (FV) deficiency (< 50%) and Aprotinin, Protamine and/or direct thrombin inhibitor (DTI) treatment are also interfering with the predicate device. On the other hand, Lupus Anticoagulants (LA) which can lead to test failure or misleading results with the predicate device and other comparable devices for FV Leiden APC Resistance screening has no influence on the discrimination power of the device. This has well been demonstrated in the CIMCLD/AKH study. Thus in this respect, the submitted device is clearly superior to the predicate device.

The kit and its reagents have shown to be very stable under different conditions relevant for their use and storage. On-board stability of the reconstituted reagents is at least 24h which is equivalent or even superior to what has been claimed for the predicate device. Real time long-term stability studies for the kit and its reagents are still ongoing, but so far the kit proved to be stable for 2 years when stored unopened at 2-8°C.

Batch-to-batch variability has been demonstrated to be very low on three pilot batches of increasing size (100, 250, and 1000 device boxes) of both the basic device and the control device.

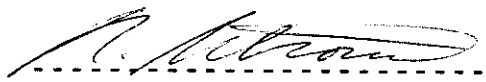
2. Brief discussion of the clinical tests submitted, referenced or relied on in the premarket notification submission for a determination of substantial equivalence

The Pefakit® APC-R Factor V Leiden was compared side-by-side with the predicate device COATEST® APC™ RESISTANCE V in clinical studies at two haematology laboratories of big central Hospitals in Europe (CIMCLD/AKH, Vienna) and the USA (Duke University Medical Center/DUMC, Durham/Raleigh NC). In these studies both tests showed to have comparable precision within the series and from day to day. Both tests were not influenced by oral coagulant treatment of the patients. In both studies the Pefakit® showed superior diagnostic sensitivity and specificity compared to the predicate device. In the CIMCLD/AKH study the influence of lupus anticoagulants on the COATEST® was clearly visible, but less so in the DUMC study. In both studies LA had no influence on the outcome of the Pefakit® assay. For all other possible interference factors included in these studies no correlation could be found between patient parameters and test outcome.

3. Conclusions drawn from the non-clinical and clinical tests that demonstrate that the device is as safe, as effective, and as well or better than the legally marketed device identified in part A (3)

Pefakit® APC-R Factor V Leiden and the predicate device COATEST® APC™ RESISTANCE V have the same intended use and can be used with the same patient groups. Both tests can be used on and adapted to a wide range of semi-automated and automated blood coagulation analyzers with mechanical and/or optical detection principle. They are thus considered to be substantially equivalent in terms of intended use, method, safety of use and overall performance characteristics.

In direct comparison with the predicate device in clinical trials the Pefakit® APC-R Factor V Leiden showed to have a higher diagnostic sensitivity and a better discrimination of the different genotypes. Even in patients with high titres of lupus anticoagulants a good test performance and genotype discrimination could be obtained.



Reto Schöni, Ph. D.

September 30, 2004

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Pentapharm Ltd.
c/o Ms. M. Elisabeth Bierman
Morgan, Lewis & Bockius LLP.
1111 Pennsylvania Avenue., NW
Washington DC 20004

DEC 22 2004

Re: k042762
Trade/Device Name: Pefakit® APC-R Factor V Leiden
Regulation Number: 21 CFR 864.7925
Regulation Name: Partial thromboplastin time tests
Regulatory Class: Class II
Product Code: GGW
Dated: December 7, 2004
Received: December 9, 2004

Dear Ms. Bierman:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,

Robert L. Becker, Jr., M.D., Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known):

Device Name: **Pefakit® APC-R Factor V Leiden**

Indications for Use:

The device is a plasma based functional IVD assay for the determination of resistance to activated protein C caused by the factor V Leiden mutation (FV:Q506) on automated and semi-automated blood coagulation analyzers using mechanical or optical detection principle.

Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

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Office of In Vitro Diagnostic Device Evaluation and Safety

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